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TO: Commissioner for Patents
Attn: Examiner K. Padmanabhan
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Washington, D.C. 20231

FROM: John J. Gresens

OUR REF: 07500.0392USWO
TELEPHONE: (612) 332-5300

Total pages, including cover letter: 85

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Title of Document Transmitted: Request for Continued Examination, Petition for Extension of Time, Amendment and Response and Declaration of Bernard Rees Smith

| | |
|---|---|
| Applicant: | BURNE, et al. |
| Serial No.: | 09/582,524 |
| Filed: | June 27, /2000 |
| Group Art Unit: | 1641 |
| Our Ref. No.: | 07500.0392USWO |

Please charge Deposit Account No. 13-2725 in the amount of $385 for the RCE filing fee and $475 for a three-month extension of time. Please charge any additional fees or credit overpayment to Deposit Account No. 13-2725. Please consider this a PETITION FOR EXTENSION OF TIME for a sufficient number of months to enter these papers, if appropriate.

By: _____
Name: John J. Gresens
Reg. No.: 33,112

I hereby certify that this paper is being transmitted by facsimile to the U.S. Patent and Trademark Office on the date shown below.

Peggy VerMeulen Grove
Signature

2/24/04
Date

2 of 2

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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

| | | | |
|---|---|---|---|
| Applicant: | Burne et al. | Examiner: | Padmanabhan |
| Serial No.: | 09/582524 | Group Art Unit: | 1641 |
| Filed: | June 27, 2000 | Docket No.: | 7500.392USWO |
| Title: | ASSAYS FOR AUTOANTIBODIES | | |

DECLARATION OF BERNARD REES SMITH
UNDER 37 C.F.R. §1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

I, Bernard Rees Smith, residing at Richmond House, Druidstone Road, Old St Mellons, Cardiff, CF3 6XD, a citizen of the United Kingdom, hereby declare:

1. I am one of the inventors of Application Serial No. 09/582524 filed on June 27, 2000 with the United States Patent and Trademark Office.

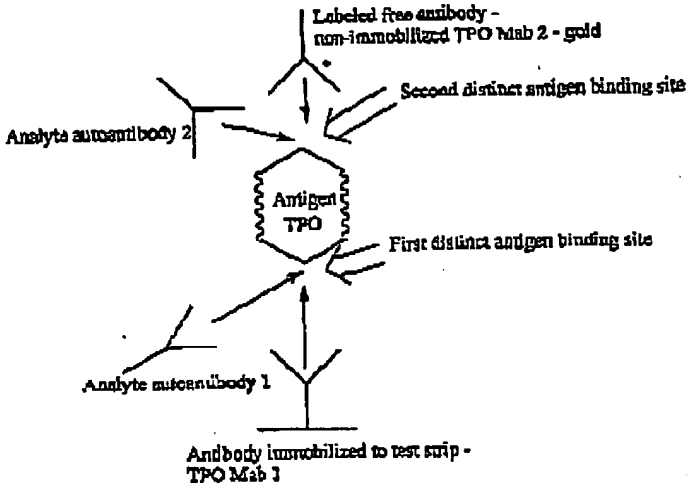
2. I am presently the Managing Director of RSR Limited and have held that position since 1982. I have extensive knowledge in the field of immunology and attach a copy of my Curriculum Vitae as Exhibit A, which shows my experience as a scientist from 1965 to date, especially in the area of the present invention.

3. I have read the Office Action mailed August 26, 2003 concerning this application.

4. I assert the assay of the invention, covered by claims 168 and 198 provides surprisingly better results than that of the prior art. The following example tested the same samples using (a) an assay according to the invention as covered by claims 168 and 198 where a double perturbation of binding is seen further to the presence analyte autoantibodies 1 and 2, and (b) an assay where a single perturbation of binding is seen, which single perturbation of binding can be correlated with the single perturbation of binding associated with the prior art assays of Bergman (US 5501955). Assay (a) can be represented by the following diagram and represents

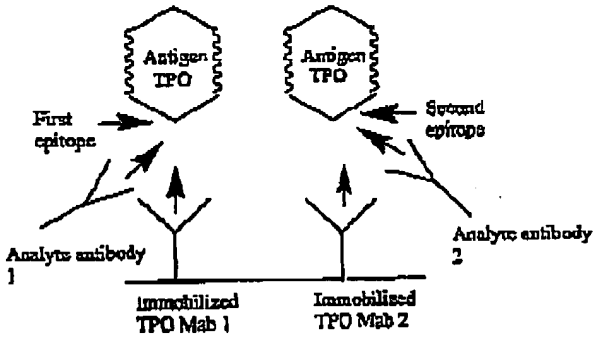
the subject matter of claims 168 and 198, wherein as indicated above a double perturbation of binding is seen further to the presence analyte autoantibodies 1 and 2:

Assay a




Assay (b) represents an assay where a single perturbation of binding is seen, which single perturbation of binding can be correlated with the single perturbation of binding associated with the prior art assays of Bergman:

Assay b




It can be appreciated from the above that in both assays (a) and (b) the same autoantibody-antigen, and Mab-antigen, interactions are being observed. However, assay (a) is such that the interactions are incorporated into a single assay binding system on the strip.

whereas in assay (b), two assay systems on the test strip are employed. Most importantly, for (a) this results in a double perturbation in binding of antigen TPO to the strip by virtue of analyte autoantibodies 1 and 2 respectively interacting with the above illustrated first and second binding sites of antigen TPO, whereas for (b) a single perturbation in binding of antigen TPO to the strip is respectively seen at immobilized TPO Mab 1 and immobilized TPO Mab 2 by virtue of analyte autoantibodies 1 and 2.

Table 1 provides the results from the two assays.

Table 1

| Test sample NIBSC 66/387 diluted in whole blood | Results with assay | |
|---|---|---|
| U/mL | (a) | (b) |
| 0 | - | - |
| 3 | - | - |
| 10 | + | - |
| 20 | + | - |
| 30 | + | + |
| 50 | + | + |

(a): Assay with TPO Mab 1 immobilized on the strip, non-immobilized TPO Mab 2–gold (label) and non-immobilized TPO. TPO Mab 1 and TPO Mab 2 interact with distinct autoantigenic epitopes on TPO;

(b): Assay with TPO Mab 1 immobilized on the strip, TPO Mab 2 immobilized on the strip and non-immobilized TPO–gold (label).

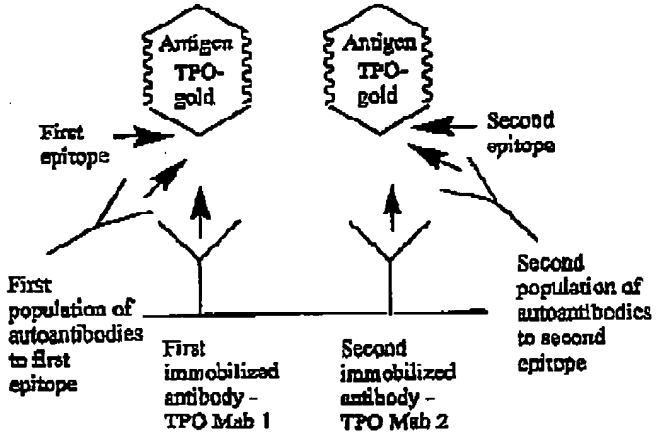
The above described double perturbation of autoantibody binding that is seen with assay (a) is of particular significance in that sensitivity of autoantibody detection in a patient sample is improved. This can be seen by reference to the results given in Table 1, where for assay (a) 10 U/mL of test sample NIBSC 66/387 can be detected, whereas for assay (b) it is only possible to detect 30 U/mL of test sample NIBSC 66/387. This improved level of autoantibody detection can be important where lower levels of autoantibody may be present in a patient sample for detection, and where such autoantibodies although present at low concentrations are indicative of autoimmune disease.

For the prior art test tube incubation techniques described by Bergman, as previously advised Bergman does not allow for autoantibody detection by synchronous competitive

inhibition of antibody binding at first and second sites on the antigen. Therefore, an assay of the invention, assay (a), provides a rapid assay for use at the point of patient care (avoiding the hitherto need to take blood samples from a patient for remote laboratory analysis, which has proven costly both in terms of time and laboratory personnel). As explained above, this can now enable detection of lower levels of autoantibody present in a patient sample and thus provide a reliable diagnosis of autoimmune disease.

The Examiner should appreciate from the above that a significant clinical advance is achieved by this invention, enabling autoantibody detection to be carried out at the point of patient care and with improved sensitivity levels.

5. I also believe that an assay, as represented by claims 184 and 211 provides significant, and unexpected advantages over the prior art. The following example provides results from an assay, as represented by claims 184 and 211. The assay can be represented by the following diagram.




This assay employs first and second immobilized antibodies allowing the detection of distinct autoantibody populations on a test strip. Looking at the test tube incubation assays of Bergman, the idea of detecting first and second analytes would have been meaningless in the context of the test tube conditions employed, given the inability to detect and distinguish between different analytes under such conditions. This assay is, therefore, clearly advantageous in allowing first and second autoantibody populations to be distinguished and detected, whereby

the test strip allows first and second detection zones to be monitored by virtue of immobilized TPO Mab 1 and TPO Mab 2 respectively provided at discrete locations on the test strip.

The results can be seen in Table 2 below.

Table 2

| Patient Sample Code | Serum TPOAb level by RIA (U/mL NIBSC 66/387) | Results using immunochromatographic strip containing TPO Mab 1 and TPO Mab 2 immobilized on the strip in different positions. Inhibition of TPO-gold binding to:- | |
|---|---|---|---|
| | | Mab 1 | Mab 2 |
| A | 80 | - | + |
| B | 1240 | - | + |
| C | 95 | - | + |
| D | 1265 | - | + |
| E | 23 | +weak | +strong |
| F | 135 | - | + |
| G | 140 | - | + |
| H | 140 | - | + |
| I | 55 | - | + |
| J | 220 | - | + |
| K | 55 | + | + |
| L | 65 | + | + |
| M | 260 | + | + |
| N | 1025 | + | + |
| O | 22 | + | - |
| P | 44 | + | - |
| Q | 258 | + | - |
| R | 66 | + | - |

The above detection and identification of first and second autoantibody populations can be of particular significance given that a heterogeneous autoantibody population of different compositions is generally formed in autoimmune disease. In this way, by detecting autoantibodies to more than one epitope as achieved by the assay of the invention, wherein at least first and second autoantibody populations can be detected and identified, this would enable a more reliable diagnosis of autoimmune disease to be achieved. For example, in prior art assays where only one autoantibody population to a single epitope region was detected, autoantibodies to a different epitope could remain undetected despite being indicative of autoimmune disease and as such misdiagnosis as to the presence of autoimmune disease could occur. Given the

above complexity of the autoimmune response and clearly the heterogeneous nature of the autoantibody population which can recognize different epitopes, it is desirable and indeed often necessary that more than one autoantibody population can be detected and reliably identified in a test assay.

6. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: 20th February 2004

23552
PATENT TRADEMARK OFFICE

# CURRICULUM VITAE

## BERNARD REES SMITH

Bernard Rees Smith

**UNIVERSITY EDUCATION:**

| | |
|---|---|
| B.Sc. | Department of Chemistry, University of Sheffield 1965 |
| Higher Degrees: Ph.D. | Department of Pharmacology, University of Sheffield 1968 |
| D.Sc. | Faculty of Science, University of Sheffield 1986 |
| Special Awards: | Harington De Visscher prize of the European Thyroid Association (in recognition of outstanding contributions to thyroid research) 1984 |
| | Honorary member of the Japan Endocrine Society 1992 |
| | RSR Ltd. received Queen's Awards for Export Achievement 1987, 1991 and 1995 |
| | Lissitzky Career Award of the European Thyroid Association in recognition of life-long contribution to thyroid research 1999. |

**PREVIOUS APPOINTMENTS:**

| | |
|---|---|
| 1970-1972 | Medical Research Council of Canada Post-Doctoral Fellow in the Department of Biochemistry, University of Toronto |
| 1972-1976 | Lecturer in the Departments of Medicine and Clinical Biochemistry, University of Newcastle upon Tyne |
| 1976-1980 | Wellcome Senior Lecturer in the Departments of Medicine and Clinical Biochemistry, University of Newcastle upon Tyne |
| 1980-1982 | Senior Lecturer, Department of Medicine, University of Wales College of Medicine, Cardiff |
| 1982-1995 | Reader in Endocrine Immunology, University of Wales College of Medicine |

**PRESENT APPOINTMENTS:**

Honorary Senior Lecturer, University of Wales College of Medicine (from 1995)

Managing Director, RSR Ltd., Avenue Park, Pentwyn, Cardiff, CF23 8HE (from 1982)

## SUMMARY OF MAJOR RESEARCH CONTRIBUTIONS

Structural analysis of long-acting thyroid stimulator and characterisation of its receptor in the thyroid.

Analysis of inter-domain interactions in immunoglobulin G.

Demonstration that Graves' IgG contains antibodies which interact directly with the thyrotrophin (TSH) receptor and that these antibodies are responsible for Graves' hyperthyroidism.

Development of radioreceptor assays for TSH receptor antibodies.

Analysis of the role of TSH receptor antibodies in controlling thyroid function in ophthalmic Graves' disease

Development of techniques to study TSH receptor antibody, thyroglobulin antibody and microsomal antibody production in culture and application of these techniques to investigate factors which control thyroid autoantibody synthesis.

Demonstration that the various forms of treatment for Graves' disease have marked effects on TSH receptor antibody synthesis and that these effects are related to the outcome of therapy.

Determination of the structure of thyroid microsomal antigen/thyroid peroxidase.

Purification of the TSH receptor by affinity chromatography and characterisation using photoaffinity labelling.

Demonstration that a water soluble fragment of the TSH receptor contains binding sites for both TSH and TSH receptor antibodies.

Determination of the structure, molecular size and shape of the TSH receptor.

Production of the first human monoclonal thyroglobulin autoantibodies.

Production of the first human monoclonal TPO autoantibodies.

First successful application of the combinatorial repertoire approach to the production of recombinant human thyroid autoantibodies.

Demonstration that 21-hydroxylase is a major adrenal autoantigen and development of assays for 21-OH autoantibodies.

Determination of the variable region sequences of monoclonal and recombinant human thyroid autoantibodies and assessment of the relationship between sequence and epitope specificity.

Demonstration that autoantibodies to 17α-hydroxylase and to cytochrome p450scc are the 2 components of steroid producing cell autoantibodies.

Development of the first ELISA for TSH receptor autoantibodies.

Development of the first sensitive and specific non-isotopic assays for autoantibodies to GAD and to IA2.

## GRANTS AND AWARDS FOR RESEARCH

| | |
|---|---|
| 1973 and 1974 | £9,133 from the Medical Research Council and £700 from the Ernest and Minnie Dawson Cancer Trust to support studies on the characterisation of the thyroid cell surface. |
| 1975 | £12,000 from the Medical Research Council in the form of a training fellowship for Dr. T. F. Davies to study thyroid-stimulating antibodies in Graves' disease. |
| | £13,477 from the Medical Research Council to support studies on the synthesis of thyroid-stimulating antibodies (with Professor R. Hall). |
| 1977 | £21,077 from the Wellcome Trust to support studies on an experimental model for Graves' disease (with Professor Hall). |
| | £18,337 from the Medical Research Council for a project entitled "Purification and characterisation of thyroid-stimulating antibodies" (with Professor R. Hall). |
| | £20,600 from the Cancer Campaign for the study of serum thyroid-stimulating antibodies, thyroglobulin and the thyroid cell in patients with thyroid cancer (with Mr. W. M. Ross and Professor R. Hall). |
| | £11,943 from the Research Committee of the Newcastle Area Health Authority (Teaching) to support an investigation into structure-activity relationships in thyrotrophin and thyroid-stimulating antibodies. |
| 1978 | £5,957 from the Research Committee of Newcastle Area Health Authority (Teaching) for a study of the TSH receptor at the ultrastructural level. |
| | £15,000 from the Medical Research Council in the form of a training fellowship for Dr. A. M. McGregor to study lymphocyte function in autoimmune thyroid disease |
| 1980 | £32,515 from the Medical Research Council for a project entitled "the relationship between receptors for long-acting thyroid-stimulator and thyrotrophin" (with Professor R. Hall). |
| | £20,000 from the Medical Research Council in the form of a training fellowship for Dr. A. P. Weetman to study autoantibody synthesis *in vitro*. |
| | £16,097 from the Welsh Office scheme for the development of health and social research to support an investigation into prediction of relapse in Graves' disease |

| | |
|---|---|
| 1981 | £3,565 from the Sir Stewart Halley trust to study the influence of antithyroid drugs and sex hormones on thyroid autoantibody synthesis in Graves' disease (with Dr. A. F. Weetman and Professor R. Hall). |
| | £90,000 from the Wellcome Trust in the form of a Wellcome Senior Research Fellowship for Dr. A. M. McGregor to study the production and properties of monoclonal human thyroid autoantibodies (with Professor R. Hall). |
| 1982 | £26,000 from the Welsh Office to investigate the properties of TSH receptor binding and thyroid stimulating antibodies in Graves' disease. |
| 1983 | £48,000 from the Medical Research Council to support an investigation into photoaffinity labelling of the thyrotropin receptor. |
| 1984 | £44,000 from the Medical Research Council to support an investigation into a water soluble fragment of the TSH receptor. |
| 1990 | £73,000 from the Medical Research Council to support an investigation of autoimmune thyroid disease at the molecular level in collaboration with the University of Sheffield (with Professor D. R. Burton). |
| 1991 | £116,838 from the Science and Engineering Research Council to meet half the costs (the remaining funding to be made by RSR Ltd., Cardiff) of a 3-year project in collaboration with the University of Bath to produce recombinant TSH receptor. The project to be administered by the Teaching Company. |
| 1994 | from the Science and Engineering Research Council for a CASE research studentship in collaboratorion with the University of Sheffield to work on the analysis of human autoantibodies in thyroid disease. |
| 1997 | from the Medical Research Council for a 3-year industrial collaborative studentship (with the Universities of Bath and St. Andrews) to work on the crystallisation of thyroid peroxidase. |

**RESEARCH FUNDING AND RSR LTD.**

RSR Ltd. was formed in 1982 with the aim of providing funds for academic research from the manufacture and sale of reagents for diagnostic kits. At first, the Company operated in the Department of Medicine, University of Wales College of Medicine and paid the College a percentage of sales. In 1985, RSR's manufacturing operations moved to a purpose-built site at Penrwyn Cardiff and in 1994, construction and operation of a basic research facility at Llanishen Cardiff was completed. RSR provided most of the funds for running the Endocrine Immunology Unit in the Department of Medicine, University of Wales College of Medicine between 1985 and 1994.

RESEARCH STAFF (FIRS Laboratories, Llanishen, Cardiff)

Jadwiga Furmaniak MD, PhD (Director)
Michael Powell BSc, PhD (Head of Molecular Biology)
Jane Sanders BSc, PhD (Head of Cell Biology)
Ian Matthews, BSc, PhD (Senior Scientist)
Tonya Richards BSc (Scientific Assistant)
Carol James HND (Administrator)
Caryl Morteo (Laboratory Technician)
Andrew Sullivan BSc (Laboratory Technician)
Angela Kiddie BSc (Laboratory Assistant)
Karen Brereton BA (Laboratory Assistant)
Michele Evans BSc (Laboratory Assistant)
Marie-Andrée Amoroso PhD (Scientific Assistant)
Shu Chen MD, PhD (Project Leader)
Simon Arch (Laboratory Help)
Clare Arnold BSc (Scientific Assistant)
Helen Brooking BSc (Scientific Assistant)
Hilde Depraetere BSc, PhD (Scientific Assistant)
Marleen Groenen BSc (Laboratory Technician)
Rachel Hewer BSc (Laboratory Technician)
Jennifer Jeffreys BSc (Laboratory Technician)
Ling Jiang BSc (Laboratory Technician)
Rossitza Ananieva-Jordanova MD (Scientific Assistant)
Vivienne McGrath (Laboratory Technician)
Carol Belton BSc (Laboratory Technician)
Mirena Noyvirt MD (Scientific Assistant)
Emma Roberts BSc (Laboratory Technician)
Kasemsri Small MPhil (Laboratory Technician)

## CURRENT VISITING FELLOWS

Hanna Stankowiak-Kulpa MD, PhD (Medical Faculty, University School of Medicine, Poznan, Poland) (2002-date)

Takashi Nakamatsu MD (Second Department of Internal Medicine, University of the Ryukyus, Okinawa, Japan) (2001-date)

## PREVIOUS VISITING FELLOWS

Yoshihiro Kajita MD (Department of Medicine, Nantan General Hospital, Kyoto, Japan) (1983-1984)

Jadwiga Furmaniak-Wehr MD, PhD (Department of Endocrinology, School of Medicine, Poznan, Poland) (1984-1985)

Yoshiyuki Nakajima MD (Department of Medicine, Nantan General Hospital, Kyoto, Japan) (1986-1988)

Naofumi Fukuma MD (3rd Department of Internal Medicine, Hamamatsu University School of Medicine, Shizuoka, Japan (1988-1990)

Faisal Abdalla Hashim MB, BS, PhD (Faculty of Medicine, University of Khartoum, Sudan) (1991)

Noriko Wakabayashi, (Cosmic Corporation, Tokyo, Japan) (1992)

Janusz Bednarek MD (Department of Endocrinology, School of Medicine, Poznan, Poland) (1991-1992)

Masateru Horimoto MD, PhD. (Endocrinology Unit, Department of Internal Medicine, Kansai Medical University, Osaka, Japan), (1991-1992)

Yoshinori Kiso MD (Endocrinology Unit, Department of Internal Medicine, Tohoku University School of Medicine, Sendai, Japan) (1991-1992)

Aleksandra Baumann-Antczak MD, (Department of Endocrinology, School of Medicine, Poznan, Poland) (1992-1993)

Joanna Sawicka MD PhD (Department of Endocrinology, School of Medicine, Poznan, Poland) (1993-1994)

Takayuki Asawa MD, PhD (Department of Gerontology, Endocrinology and Metabolism, Shinshu University School of Medicine Japan) (1992-1995)

Maria Sylvia Perez BSc (Argentine Foundation for Endocrinology, Buenos Aires, Argentina) (1994-1996)

Ryoji Kato MD, PhD (Department of Medical Technology School of Allied Medical Science, Shinshu University School of Medicine Japan) (1994-1995)

Julio César Rodriguez González BSc (National Institute of Endocrinology, Havana, Cuba) (1995)

Hideaki Tanaka MD, PhD (Department of Internal Medicine, Faculty of Medicine, University of the Ryukyus, Okinawa, Japan) (1995-1997)

Alison Bailey BSc, Department of Molecular Biology and Biotechnology, University of Sheffield (CASE student 1993-1996)

Katarzyna Ziemnicka MD, PhD (Department of Endocrinology, School of Medicine, Poznan, Poland) (1995-1997)

Masayuki Maruyama MD, PhD (Second Department of Surgery, Shinshu University School of Medicine, Matsumoto, Japan) (1996-1998)

Pawel Gut MD, PhD (Department of Endocrinology, School of Medicine, Poznan, Poland (1998-1999)

Masato Masuda MD, PhD (Second Department of Internal Medicine, Faculty of Medicine, University of the Ryukyus, Okinawa, Japan) (1997-1999)

Shu Chen MD, MS (Institute of Endocrinology, Tianjin Medical College, People's Republic of China) (1995-1998).

Yasuo Oda MD, PhD (Second Department of Internal Medicine, Osaka University Medical School, Japan) (1995-2000)

Elaine Hendry BSc., Centre for Biomolecular Sciences, University of St. Andrews (CASE student 1997-2000)

Nobuki Hayakawa MD, PhD (Department of Internal Medicine, Fujita Health University School of Medicine, Aichi, Japan) (1999-2001)

Chiara dal Pra MD, PhD. (Department of Medical and Surgical Sciences, University of Padova, Italy) (2000-2001)

Ken Nakachi BM, (Second Department of Internal Medicine, University of the Ryukyus, Okinawa, Japan) (1999-2002)

## STUDENTS OBTAINING HIGHER DEGREES:

**PhD** Pamela Povey
Characterisation of the thyroid cell surface (1979)

Sandra McLachlan
Thyroid autoantibody synthesis in man (1980)

Vaughan B. Petersen
Studies with the cytochemical bioassay for thyroid stimulators (1980)

F. A. Hashim
Studies on the TSH receptor and TSH receptor antibodies (1987)

Sylvia Fowler
Characterisation of thyroid autoantigens (1994)

Louise Prentice
Molecular and genetic basis of thyroid autoimmunity (1995)

Fiona Grennan Jones
Expression and characterisation of recombinant human thyroid peroxidase produced in the baculovirus expression vector system (1997)

Shu Chen
A study of humoral autoimmunity in autoimmune adrenal disease (1998)

**MD** T. F. Davies
The thyrotrophin receptor (1977)

C. S. Teng
TSH receptor binding immunoglobulins in patients with thyroid disease (1980)

E. D. Mukhtar
Thyroid stimulating immunoglobulins in thyroid disease (1980)

A. M. McGregor
Lymphocyte function in autoimmune thyroid disease (1981)

F. M. Creagh
Thyrotrophin receptor antibodies in Graves' disease (1985)

**MSc** K. C. Chan
A study of disulphide bond formation in immunoglobulin G (1974)

S. Karam
The binding of human chorionic gonadotrophin to the rat testis (1979)

**MPhil** Peter Burne
Rapid point-of-care tests for thyroid autoantibodies (2002)

**MEMBERSHIP OF LEARNED SOCIETIES:**

The Society for Endocrinology

The British Thyroid Association

The American Thyroid Association

The American Endocrine Society

The Biochemical Society

The European Thyroid Association

The American Association for Clinical Chemistry

Honorary Member - Japan Endocrine Association

## PAPERS PRESENTED TO LEARNED SOCIETIES:

The interaction between LATS and thyroid tissue *in vitro*.
The Medical Research Society London 1968

Characterisation of the LATS binding protein from human thyroid tissue.
The Royal Society of Medicine London 1970

Purification and characterisation of LATS gamma G binding protein.
The Sixth International Thyroid Conference Vienna 1970

Subunit interactions in immunoglobulin G.
The Federation of Canadian Biological Societies Ottawa 1972

The thyroid-stimulating hormone receptor and thyroid-stimulating antibodies
The Society for Endocrinology London 1974

Characterisation of the human thyroid-stimulating hormone receptor
The Biochemical Society St. Andrews 1974

Thyroid-stimulating immunoglobulins and the control of thyroid function
The Thyroid Club London 1975

Thyroid-stimulating immunoglobulins in Graves' disease
Postgraduate Medical Federation Endocrinology course London 1975

The thyrotrophin receptor
National Institute of Health (Bethesda Maryland) Endocrinology seminar 1975

Antibody and hormone binding to the thyrotrophin receptor
University of Chicago Medical School seminar 1975

Thyroid-stimulating immunoglobulins and hyperthyroidism
Seventh International Thyroid Conference Boston 1975

Thyrotrophin receptor antibodies
Schilddruse Homburg West Germany 1975

Thyroid-stimulating antibodies
Symposium Lecture, Fifth International Congress of Endocrinology Hamburg 1976

Partial characterisation of solubilised human and porcine TSH receptors
The Society for Endocrinology London 1977

Antibodies to hormone receptors
Thyroid Club London 1978

The TSH receptor
National Institute of Health (Bethesda Maryland) Endocrinology seminar 1978

## PAPERS PRESENTED TO LEARNED SOCIETIES (CONT.)

TSH receptor antibodies
Toronto Endocrine Society Toronto Canada 1978

Membrane receptors for polypeptide hormones
Association of Clinical Pathologists London 1979

Thyroid autoantibody synthesis by Hashimoto thyroid lymphocytes
Thyroid Club London 1979

Thyroid-stimulating antibodies
Polish Endocrine Society 1979

Receptors for protein hormones
Polish Endocrine Society 1979

The pathogenesis of Graves' disease
Symposium lecture at the Royal Society of Medicine meeting Newcastle 1979

Treatment and the immune response in Graves' disease
Schilddruse Homburg Saar 1979

The pathogenesis of hyperthyroidism
Symposium Lecture at the Joint meeting of the Moynihan Chirurgical Club and Warren Cole Society Newcastle 1979

TSH receptor antibodies
Symposium lecture at the Acta Endocrinologica meeting Munich 1979

The TSH receptor and TSH receptor antibodies
Symposium Lecture to the Biochemical Society Cambridge 1979

Antibodies to the TSH receptor in Graves' disease
University of Rotterdam seminar 1979

TSH receptor antibodies
Symposium Lecture Sixth International Congress of Endocrinology Melbourne 1980

Multiple forms of hormone-receptor complexes
Sixth International Congress of Endocrinology Melbourne 1980

The TSH receptor in disease
Symposium on hormone receptors in disease Auckland 1980

The interaction of Graves' immunoglobulin with the TSH receptor
Eighth International Thyroid Conference Sydney 1980

Autoantibodies to peptide hormone receptors
Federation of European Biochemical Societies meeting Galway 1980

## PAPERS PRESENTED TO LEARNED SOCIETIES (CONT.)

Membrane receptors for polypeptide hormones
Royal College of Pathologists' symposium entitled "Recent advances in Endocrinology" London 1981

Interaction of Graves' IgG with affinity purified thyrotrophin receptors
Thyroid Club London 1981

Thyroid-stimulating antibodies in Graves' disease before and after treatment
European Society for Clinical Investigation symposium Basel 1981

Characterisation of the thyrotrophin receptor
14th FEBS meeting Edinburgh 1981

Why does autoimmune thyroid disease occur?
Royal College of Physicians' symposium on modern management of thyroid disease London 1981

Autoantibodies to the TSH receptor
Symposium lecture at 8th International Congress of Pharmacology Tokyo 1981

Thyroid stimulating antibodies in Graves' disease
International symposium on thyroid autoimmunity London 1981

The thyrotrophin receptor in Graves' disease
Special guest lecture to the Japanese Endocrine Society Nagasaki 1981

Structure-function relationships of the TSH receptor
CIBA foundation symposium on receptors, antibodies and disease London 1981

TSH receptor antibodies
Invited lecturer - workshop on immune responses to cell membranes and their ligands as causes of neurological disease Palm Springs 1983

Characterisation of the TSH receptor
Invited speaker: Schilddruse 1983 Homburg Germany

Antibodies to the TSH receptor in Graves' disease
Travenol lectures at the Universities of Tokyo and Kyoto 1983

Immuno-endocrinological aspects of the TSH receptor
Plenary lecture European Society for Paediatric Endocrinology Budapest 1983

Immunoprecipitation of TSH-TSH receptor complexes
British Endocrine Societies meeting Edinburgh 1984

A structure for the TSH receptor
American Thyroid Association meeting New York 1984

## PAPERS PRESENTED TO LEARNED SOCIETIES (CONT.)

Receptor diseases
Special lecture to the 17th International Congress of Internal Medicine Kyoto 1984

Measurement of TSH receptor antibodies
Association of Clinical Biochemists' meeting Buxton 1984

Lecture tour of Japan and Korea 1984
Special presentations on the TSH receptor and its role in Graves' disease at the Universities of Tokyo, Kyoto, Osaka, Nagasaki and Seoul

The TSH receptor in Graves' disease
Symposium on thyroid autoimmunity organised by the American Thyroid Association New York 1984

Autoantibodies to the TSH receptor
European Society for Immunology symposium on receptor antibodies Interlaken 1984

Graves' disease
Special lecture at Mount Sinai Hospital medical School New York 1984

TSH receptor structure
National Institutes of Health Bethesda Maryland 1984

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Inaugural meeting of the Belgian Contact group on signal molecules and their receptors Antwerp 1987

TSH receptor subunit structure
Symposium lecture at the European Congress of Endocrinology Copenhagen 1987

Thyroid Autoantigens
Introductory lecture to the European Thyroid Association meeting Lausanne 1987

The structure of the TSH receptor
First David Owen Segal thyroid lecture Mount Sinai School of Medicine, New York 1987

Lecture tour of Japan - lectures at Universities of Sapporo, Tokyo, Maebashi, Nagoya and Kyoto followed by a plenary lecture entitled "Autoantibodies to the TSH receptor" at the 8th International meeting of the Japanese Endocrine Society, Lake Biwa 1987

TSH receptor antibodies
Symposium on thyroid autoimmunity, pathophysiology and diagnosis Brussels 1988

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Symposium lecture at the 8th International Congress of Endocrinology Kyoto Japan 1988

TSH receptor structure (invited lecture)
Direct supersensitive assays for thyroid autoantibodies
Relationship between thyroid autoantibody spectrotype and IgG subclass
All presented to the Fourth Asia and Oceania Thyroid Association meeting Seoul Korea 1989

Structural analysis of the TSH receptor
International meeting on physiological regulation and biological function of thyrotropin Goslar 1989

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B and T cell epitopes on thyroid peroxidase
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Structure and Function of the TSH receptor
International satellite meeting on thyrotropin receptor antibodies, Kyoto Japan December 1992

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Thyroid autoantibodies - new methods of analysis
Lecture at Tohoku University Japan 1992

Modern aspects of Graves' disease treatment
6th Latin American Thyroid Congress Buenos Aires Argentina May 1993

Thyroid autoantigens - Dr. Roberto Soto Memorial Lecture, 6th Latin American Thyroid Congress Buenos Aires Argentina May 1993

Thyroid autoantibodies - an overview
Lecture at University of Osaka, Japan March 1994

Detection and measurement of thyroid autoantibodies
Conference on the clinical evaluation of Tg autoantibodies and TPO autoantibodies, Tokyo Japan March 1994

Thyroid Autoimmunity 1994
Lecture at the University of Kyoto Japan March, 1994

Chairman of session on TSH receptor
American Thyroid Association, September, 1994

Endocrine Autoimmune Diseases - Recent progress and Future developments
Invited speaker - Cosmic Endocrine Forum - 68th Japan Endocrine Meeting 1995

Lectures at Gunma University Medical School, Tokyo Women's Medical College, Shinshu University Medical School and SRL Japan June 1995

Welsh Association of Clinical Biochemists Llandrindod Wells 1997

TSH receptor antibody measurements by ELISA. 72nd annual meeting of the American Thyroid Association 1999.

TSH receptor autoantibodies. Invited speaker. 12th International Thyroid Congress Kyoto 2000.

TSH receptor autoantibodies - invited speaker; University of Poznan. 2000

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